Congenital Leukemia

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Abstract Congenital leukemia is a rare but a well-documented disease in which leukemic process is detected at birth or very shortly thereafter (Philip McCoy and Roy Overton, *Commun Clin Cytom* 22:85–88, 1995). These leukemias represent approximately 0.8 % of all childhood leukemias. We present a case of congenital acute myeloid leukemia manifesting from the very first day of birth. Diagnosis of acute myeloid leukemia was suspected by the presence of blasts in the peripheral blood smear and was confirmed on bone marrow by flowcytometry. Karyotyping revealed Trisomy 21.

Keywords Congenital leukemia · Downs syndrome · Transient myeloproliferative disorder

Introduction

Congenital leukemias (CL) are a group of hematologic diseases that originate in utero, and the leukemic process is evident at delivery of the infant or within a short time period after delivery [1]. It is a very rare disease and is seen in one per five million births [2]. Most CL are myeloid in origin unlike pediatric leukemias which are usually lymphoid. Only few cases of Down syndrome with congenital leukemia have been reported in the literature; these need to be differentiated from transient myeloproliferative disorder

which is also commonly seen in children with Downs Syndrome [3].

Case Report

Our case is a premature male infant born at 33 weeks gestation with a birth weight of 1.6 kgs. He was delivered vaginally uneventfully and was shifted to the Neonatal ICU. The mother had history of fever following multiple bee stings 2 weeks prior to the onset of premature labour.

Our case is the second born to a non-consanguineous couple where paternal age is 49 years and maternal age 36 years. There was history of unexplained spontaneous abortion at 20 weeks of gestation in 2010. Neither parent nor any family member gave significant history for any chronic illness or malignant disease except for diabetes in several members of the family. The antenatal period was uneventful with all antenatal laboratory workup within normal range. History of maternal fever, rash or lymphadenopathy and tests to rule out Syphilis and TORCH infections were emphasized upon. Both parent's blood group was B Positive and there was no history of the mother receiving any blood transfusion earlier.

Physical examination after birth revealed mild hypotonia, limb disproportion and slanting eyes. No lymphadenopathy was detected. Spleen was found to be enlarged 2 cm below the left costal margin while liver measured 2.5 cm below right costal margin. However, suckling was found to be weak. Baby passed meconium and urine within 24 h of birth.

Since the suckling reflex was weak sepsis was suspected and a routine blood examination was done on the day of birth which revealed leucocytosis with a Total Leucocyte

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Fig. 1 Peripheral blood smear (day 1) showing myeloblasts

ACCESSION NO. 101298062		AGE :	15 days	SEX :	M
CLINICAL INFORMATION:					
Chromosomal Analysis					
Metaphase Karyotyping: GTG Banding					
TEST REPORT STATUS	FINAL	RESULTS			
Method Used	: 24hr unstimulated culture				
Banding Resolution	: 450-500				
CYTOGENETIC PROFILE:					
Metaphases Counted	: 20				
Metaphases Analyzed	: 20				
Metaphases Karyotyped	: 08				
KARYOTYPE					
Total Chromosome Number	: 47				
Autosomes	: 45				
Sex Chromosomes	: 2(XY)				
OBSERVATION	: 47,XY,+21				
Interpretation					
There is an extra chromosome 21 (trisomy 21), found in all the metaphases studied.					

Fig. 2 Karyotyping report

Count of 108,000/ μ l, Hb of 19.2 gm/dl and thrombocytopenia with a Platelet count of 30,000/ μ l.

A peripheral blood smear examination showed presence of 80 % blasts with high NC ratio, moderate amount of cytoplasm, round to irregular nuclear contour, fine chromatin and 2–5 nucleoli (Fig. 1). Bone Marrow Aspiration was done which showed Blast 74 % which were strongly positive for Myeloperoxidase.

Immunophenotyping showed the blasts to be strongly positive for Myeloid Markers (CD33, CD34, CD45, CD117, HLA DR). Blasts were also found to be positive for CD 7 which is a T Cell marker. It is a well known fact that CD 7 is a common aberrant marker in acute myeloid leukemias.

Karyotyping revealed Trisomy 21 (Fig. 2), thereby affirming the physical features to be consistent with Down

syndrome. VDRL Test of baby was negative and this ruled out Syphilis.

A repeat routine blood examination on 18th day showed Total Leucocyte Count 98,000/ μ l, platelets further reduced to 10,000/ μ l and blasts comprising 70 % of all WBC.

All other laboratory workup of baby was within acceptable range. However the baby failed to gain weight and weight on 21st day of birth was 1.5 kg. The baby seemed to be responding favourably to the supportive care and was on exclusive breast feeding till 23rd day of age when he suddenly developed unexplained abdominal distention and died of cardiorespiratory arrest on 26th day of birth.

Discussion

Congenital leukemia (CL) is a term applied to leukaemia diagnosed at birth or within the first month of life [4]. It is a rarity [5]. Our case presented from the very first day of birth and fulfilled the criteria for the diagnosis of congenital leukemia [6] which include- Proliferation of immature white cells; Infiltration of these cells into bone marrow; Absence of any other disease that can cause leukemoid reaction mimicking leukemia i.e. congenital syphilis, Blood group incompatibility and TORCH infection. Etiological considerations in CL have included chromosomal defects, intrauterine environmental insults, viral infections and exposure to radiation in pregnancy [7]. Chromosomal abnormality (Trisomy 21) was detected in our case.

The clinical signs of leukemia may be evident at birth with hepatosplenomegaly, petechiae and ecchymosis. Leukemic cell infiltration into the skin (leukemia cutis/chloroma) is commonly found when the disease appears at birth and has also been noted in still born premature infants with leukemia [5]. At birth many of the infants have respiratory distress from either leukemic infiltration in the lungs or atelectasis. In those infants in whom the disease develops within first month (not at birth), the symptoms are ill defined with low grade fever, diarrhea, hepatomegaly and failure to gain weight. Leukemia cutis is less common [7]. However, our case was a premature infant presenting at birth, he showed no symptoms of lethargy, seizure, bleeding manifestations or breathing difficulty. On examination, low set eyes, limb disproportion and splenomegaly were noted. No skin manifestations were found. Blood and bone marrow examination revealed blasts with severe thrombocytopenia. Blasts were confirmed to be as myeloid on cytochemistry and flowcytometry.

The cytogenetics of congenital leukemia has been studied, and several different abnormalities have been identified, including monosomy 7, trisomy 9, Down

syndrome, 11q23, t(9;18), t(11;19), t(9;11), and t(X;6) [1]. Subtle cytogenetic abnormalities may occur more commonly in the affected infants and their parents, when studied with newer cytogenetic techniques [8]. Survival time in congenital leukemia is brief. Many infants die of respiratory distress secondary to pulmonary leukostasis and bronchopneumonia [9]. The exact cause of death in our case remained unknown as he died suddenly with abdominal distension; possibly of septicemia. It is important to differentiate congenital leukemia from other leukoerythroblastic conditions which are seen in response to bacterial infections, hypoxemia and severe haemolysis in the neonates. Most important differential diagnosis is transient myeloproliferative disease (TMD) associated with Down syndrome. Transient myeloproliferative disease has been identified by its unique characteristics of paucity of leukemic blasts in the marrow, variable pancytopenia, a propensity for mild to life-threatening hepatic infiltration, and typically a spontaneous regression without any intervention help [10]. Also earlier reports have found the blasts in transient myeloproliferative syndrome to be negative for Myeloperoxidase [11]. Our child hardly showed any improvement in his blood picture and succumbed to the leukemic process by 3.5 weeks of age. Other differential diagnoses are congenital syphilis, intrauterine viral disease, ABO/Rh incompatibility, all of which have been ruled out.

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